

Cirrhosis and hepatoma in alcoholics

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EDITORIAL SYNOPSIS This paper describes the development of hepatoma in cirrhosis of the alcoholic as seen in east London. The incidence was surprisingly high (30%) (25 of 84 cases) and was noticed especially in those who had given up alcohol before death and had developed a coarse nodular type of cirrhosis.

The cause of cirrhosis in alcoholics is unknown but nutritional deficiencies have been invoked as being important, largely on the basis of experimental work in animals. This includes the production of fatty liver and cirrhosis in rats by diets deficient in lipotropic substances such as choline and methionine (Blumberg and McCollum, 1941) and by low-protein diets (Rich and Hamilton, 1940). The recent finding of folic acid deficiency in a group of alcoholics (Herbert, Zalusky, and Davidson, 1963) has highlighted the observation that vitamin B₁₂ and folic acid facilitate endogenous choline synthesis in some animals (Klatskin, 1961). Observations in man have failed to show any consistent relationship between malnutrition and cirrhosis, although the poor nutritional state of many alcoholics is not questioned. No conclusive link between kwashiorkor, a disease of the liver due to protein deficiency, and cirrhosis has been established (Higginson, Grobbelaar, and Walker, 1957). Cirrhosis is rare in conditions associated with poor nutrition except for chronic alcoholism and ulcerative colitis in which other factors are thought to be important for the development of liver disease (Palmer, Kirsner, Goldgraber, and Fuentes, 1964). However, improvement has been shown to follow the giving of a high-protein diet (Patek and Post, 1941), even when alcohol is continued (Summerskill, Wolfe, and Davidson, 1957).

Jolliffe and Jellinek (1941) collected figures from a number of countries on the incidence of cirrhosis in alcoholics. Although there was wide variation between different areas, they found that cirrhosis occurred in approximately 8% of chronic alcoholics, an incidence of seven times that in the general population. They also commented on the high incidence of cirrhosis in occupations associated with a high intake of alcohol, *i.e.*, in publicans, brewery

workers, commercial travellers, and dock workers. A sharp decline in the incidence of cirrhosis during prohibition in the United States was noted (Rowntree, 1927) and an increase subsequently (Schmid, 1940). These observations confirm that there is an association between alcoholism and cirrhosis, but give no clue to the cause.

This paper reports 84 patients with cirrhosis who had taken an excess of alcohol. Emphasis has been placed on the variable nature of this entity and some correlation is made between clinical and morphological features. The clinical notes, necropsy records, and liver histology of all patients with cirrhosis of the liver coming to necropsy at the London Hospital in the 50 years 1914 to 1963 inclusive have been reviewed. A number have been excluded because insufficient information or material was available. A few have been excluded because the part played by other factors, such as biliary obstruction and heart failure, was difficult to determine. One hundred and eighty-two cases were acceptable as fulfilling the necessary criteria, namely, (1) sufficient information to determine whether there was a previous history of excessive intake of alcohol, or of an illness suggestive of vital hepatitis; (2) the post-mortem description and microscopic specimens were enough evidence for it to be certain that cirrhosis was present and it was possible to determine the morphological type. Cases have been classified according to three morphological types as follows.

CLASSIFICATION OF CASES

FINELY NODULAR CIRRHOSIS This is the variety most commonly associated with excessive intake of alcohol (Baggenstoss and Stauffer, 1952; Popper, Rubin, Krus, and Schaffner, 1960; Gall, 1960a). It is characterized by small nodules, 4 mm. or less in diameter, the nodules being nearly equal in size.

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Fibrous tissue is present, the bands varying in width, but is usually distributed evenly through the liver in individual cases, coarse scars not being seen. In very active cases, sometimes termed 'florid' cirrhosis (Popper, Szanto, and Parthasarathy, 1955), fibrous tissue appears to be actively invading the nodules which show complete disorganization of the liver parenchyma with few, if any, recognizable central veins. Fat is often present, sometimes in great excess. The weight of the liver is on average higher than in other varieties of cirrhosis.

COARSELY NODULAR CIRRHOSIS In this variety the nodules are larger but the overall loss of pattern, with few normally placed central veins, resembles that seen in the finely nodular type. The nodules may be up to 1.5 cm. or more in diameter, the fibrous tissue being evenly distributed. The distinction between these two types is not always made, all cases without coarse scars being classified as portal cirrhosis of Laennec.

POST-NECROTIC CIRRHOSIS This term is justified by usage and is so well established that it will not be replaced until a term is introduced more clearly based on proven aetiology than those suggested to date. It is characterized by more variation in the size of the nodules, some being large, occasionally several centimetres in diameter. Nodules may include near normal lobules or several smaller nodules, and fibrous tissue is unevenly distributed through the liver. Coarse scars may be present and these are usually attributed to approximation of the portal tracts following parenchymal necrosis and are also thought to occur following fissures resulting from asymmetrical collapse. Histologically, the presence of approximated portal tracts and central hepatic veins is diagnostic of post-necrotic cirrhosis (Steiner, 1960a), but is often difficult to observe with certainty. Baggenstoss (1961) prefers to rely on the presence of coarse scarring and this criterion has been used in the present study. Cellular infiltration is often more marked than in other varieties of cirrhosis. Post-necrotic cirrhosis is the type most commonly thought to be associated with previous viral hepatitis.

Particular attention has been paid to the following points in the clinical notes:—Did the patient habitually take alcohol in excess? (The limits of Ratnoff and Patek (1942) were taken, *i.e.*, one quart of wine, six glasses of beer or four whiskeys, daily.) Did excess alcohol intake continue until death, or did the patient stop drinking or drastically reduce his intake some years before death? Did the patient die from liver cell failure, or did some other illness interrupt the natural history of the disease? In most patients the answer to this question was clearcut.

However, in a few cirrhosis complemented other disease in accelerating death. In these circumstances death was attributed to cirrhosis for the purpose of analysis. A particular problem was posed by bleeding from oesophageal varices. Where this catastrophe supervened in a patient seriously ill with cirrhosis, death was attributed to liver disease. However, if death could be predominantly attributed to bleeding, the patient was considered to have had the course of his illness interrupted by other factors. In general, ascites was absent in this latter group and its absence could be taken as the criterion for previously compensated cirrhosis. Only patients with a history of habitually taking alcohol in excess are reported here. There are 84 such cases, an incidence of 46% of all cases of cirrhosis in the study.

The London Hospital is situated in the East End of London. Nearby are two large breweries and most of the London docks are within a few miles. These factors may increase the incidence of alcoholism in the area and, therefore, the hospital series compared with other series in Great Britain. The hospital serves as a general hospital for this part of London and few cases have been referred from outside the area. This series represents, therefore, cirrhosis of the liver in alcoholics in the East End of London.

The distribution of cases over the decades is shown in Table I. The mean age for the whole series is 55.7 years, with a range of from 33 to 78

TABLE I
NUMBER OF CASES OF ALCOHOLIC AND NON-ALCOHOLIC CIRRHOSIS

Years	Alcoholic	Non-alcoholic	Total
1914-23	11	13	24
1924-33	24	22	46
1934-43	12	12	24
1944-53	11	26	37
1954-63	26	25	51
1914-63	84	98	182

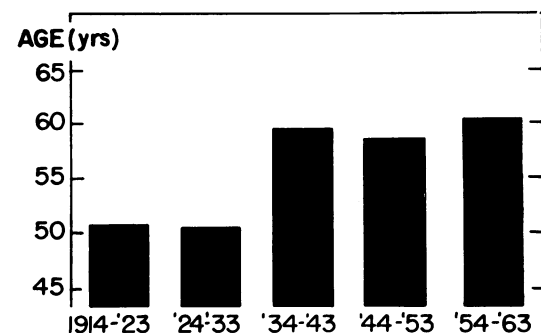


FIG. 1. Mean age at death of patients with 'alcoholic cirrhosis' over the decades 1914-1963.

years. There are 73 men and 11 women. There has been no significant change in the average age at death since 1934, the most marked increase in survival occurring between the second and third of the five decades under review (Fig. 1).

MORPHOLOGY

Forty-two cases were classified as having finely nodular cirrhosis, 25 as coarsely nodular cirrhosis, and 18 as post-necrotic cirrhosis. Thus, half did not have the finely nodular cirrhosis classically associated with excessive intake of alcohol. There is an apparent predominance of post-necrotic cirrhosis in the first decade (Table II). The effect of the patients' drinking habits is shown in Figure 2. The proportion of cases of finely nodular cirrhosis is higher in those who continued drinking as long as their illness allowed, and correspondingly, there is a higher incidence of coarsely nodular cirrhosis in patients who gave up drinking before death. Post-necrotic cirrhosis appeared not to be influenced by drinking habits and may have a different pathogenesis from the other two varieties. It is suggested that abstinence from or temperance in the intake of alcohol after a period of excess, allows regeneration with larger

TABLE II

MORPHOLOGICAL TYPE OF CIRRHOSIS

Years	Type of Cirrhosis		
	Finely Nodular	Coarsely Nodular	Post-necrotic
1914-23	3	2	6
1924-33	16	4	4
1934-43	5	6	1
1944-53	5	3	3
1954-63	13	9	4
1914-63	42	24	18

nodules than if excess alcohol intake continues to death. The presumption is that in most cases, finely nodular cirrhosis was present at the time heavy drinking was curtailed and coarsely nodular cirrhosis developed subsequently.

HEPATOMA

Some interesting points arise when the patients with primary carcinoma of the liver (hepatoma) are considered. Table III shows the incidence of hepatoma in alcoholics and non-alcoholics with cirrhosis. Hepatoma occurred in 25 out of 84 alcoholics (30%) and in 11 out of 98 non-alcoholics (11%). Parker (1957) also observed a high incidence of hepatoma in patients with alcoholic cirrhosis in a London Hospital series and this point will be discussed more fully later.

TABLE III

INCIDENCE OF HEPATOMA IN PATIENTS WITH NON-ALCOHOLIC AND ALCOHOLIC CIRRHOSIS

Years	Non-alcoholic	Hepatoma	Alcoholic	Hepatoma
1914-23	13	0	11	2
1924-33	22	4	24	6
1934-43	12	2	12	6
1944-53	26	2	11	5
1954-63	25	3	26	7
1914-63	98	11	84	25

The incidence of hepatoma in the different morphological types and the relation to drinking habits is shown in Figure 3. The incidence is much higher in those who gave up drinking, 16 out of 29 (55%), than in those who continued drinking in whom hepatoma was present in only nine out of 55 cases (16.4%). This point is made even more forcibly if a distinction is made between those dying

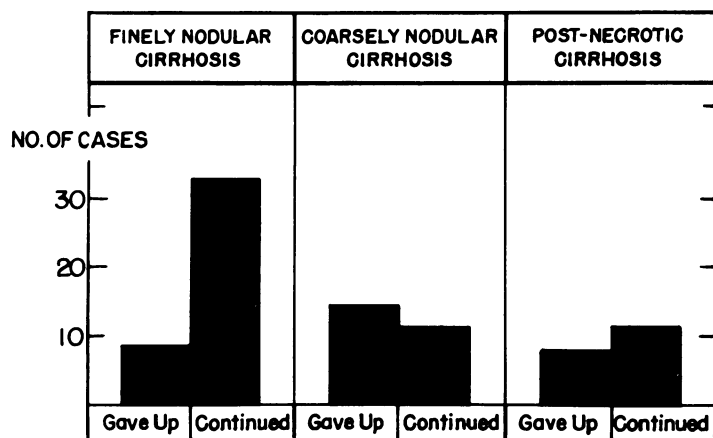


FIG. 2. Influence of drinking habits on morphological type of cirrhosis.

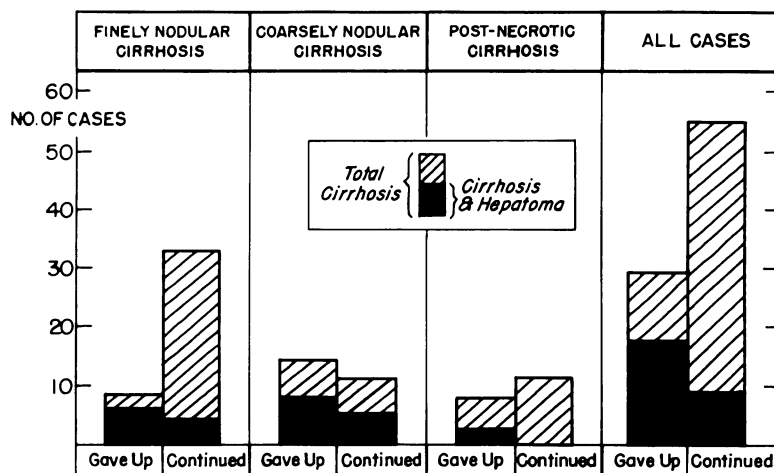


FIG. 3. Influence of drinking habits and morphology on incidence of carcinoma.

TABLE IV

INCIDENCE OF HEPATOMA IN CASES DYING OF LIVER DISEASE AND OF OTHER CAUSES

Morphology	Liver Disease		Other Causes	
	Total	With Hepatoma	Total	With Hepatoma
Finely nodular	31	11	11	0
Coarsely nodular	17	10	7	1
Post-necrotic	13	3	5	0
All cases	61	24	23	1

TABLE V

INCIDENCE OF HEPATOMA IN PATIENTS WHO GAVE UP DRINKING

Morphology	Dying of Liver Disease		Dying of Other Causes	
	Total	Hepatoma	Total	Hepatoma
Finely nodular	9	7	0	0
Coarsely nodular	9	6	4	1
Post-necrotic	6	3	1	0
Total	24	16	5	1

of liver disease and those dying of other cause (Table IV). Of 61 cases dying of liver disease, 24 had a hepatoma (39.3%) and in all these the hepatoma contributed significantly to the patient's death. In addition, if a patient abstains from, or greatly reduces, his intake of alcohol and still has the misfortune to die of liver disease, he has a 16 in 24

chance (66.7%) of dying with a hepatoma (Table V). The incidence of hepatoma is highest in coarsely nodular cirrhosis, the variety which is commonest in those who curtailed heavy drinking some years before death (Table IV). Figure 4 shows the ages at death of patients with and without hepatoma according to morphological type. The mean age for

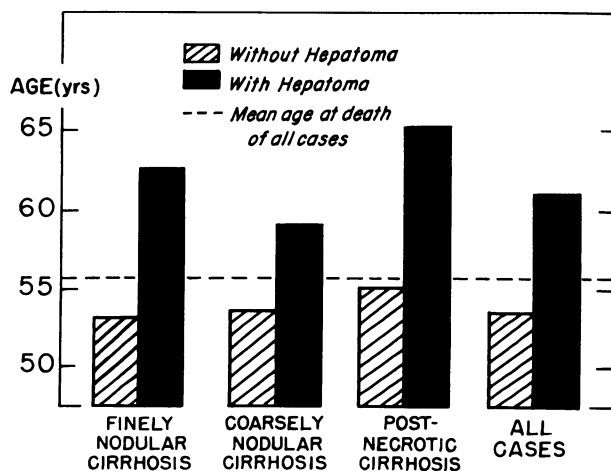


FIG. 4. Mean age at death of patients dying with and without hepatoma, according to morphological type.

cases dying without hepatoma was 53.4 years and 60.8 years for those with hepatoma.

INFLUENCE OF SEX

Parker (1957) considered that the high incidence of hepatoma in his series of patients with alcoholic cirrhosis was chiefly due to the predominance of men in this group. This point is confirmed in the present series which includes most of his cases and covers a longer period of time. There are only 11 women and the distribution through the decades is shown in Table VI. Additional points are that 10 out of the 11 cases continued heavy drinking until their terminal illness and none of these had a hepatoma. The one patient who had a hepatoma was also the oldest and had curtailed heavy drinking before death. There are 73 men in the series of whom 24 had hepatomas (32.8%). This confirms Parker's observation, but it is also suggested that some of the sex difference is due to particular factors in the small number of women in the series, *i.e.*, a high proportion continued drinking to death and most of them died younger than the usual age at which hepatoma develops.

TABLE VI

ALCOHOLIC CIRRHOSIS IN WOMEN

Year	Drinking Habits	Morphology			Hepatoma
		Finely Nodular	Coarsely Nodular	Post-necrotic	
1914-23	Drank to death (3) ¹	2		1	None
1924-33	Drank to death (6)	4	1	1	None
1934-53	No cases				
1954-63	Drank to death (1)		2		1

¹No. of cases in brackets

INFLUENCE OF VIRAL HEPATITIS

Four cases gave a history of a previous illness resembling viral hepatitis, although in a retrospective study it is difficult to be certain that the patients had not had active liver disease of the alcoholic (Phillips and Davidson, 1954). The four cases are shown in

TABLE VII

CASES OF PREVIOUS HEPATITIS IN MEN

Year	Age of Case (yr.)	Drinking Habits	Morphology	Hepatoma
1936	45	Continued to death	Coarsely nodular	None
1949	47	Continued to death	Post-necrotic	None
1955	49	Continued to death	Coarsely nodular	None
1955	55	Continued to death	Finely nodular	Yes

Table VII. All were men and the age range was from 45 to 55 years. There were two cases of finely nodular, one of coarsely nodular, and one of post-necrotic cirrhosis. There was one hepatoma in a patient with finely nodular cirrhosis who continued drinking to death. This patient was also the oldest of the four. There are too few cases here to draw any conclusion about the influence of viral hepatitis on cirrhosis, but it is interesting that although there are 18 cases of post-necrotic cirrhosis in the series, only one gave a history of previous viral hepatitis.

DISCUSSION

The cause or causes for the association between alcoholism and cirrhosis remain obscure. The very striking accumulation of fat continues to impress many authors (Popper, Szanto, and Elias, 1955; Goldberg and Thompson, 1961). It is suggested that intense focal accumulation of fat results in fatty cysts which rupture leaving an area of collapse and necrosis. Such a phenomenon has been observed in rats (Hartroft, 1950), but the failure of other experimental animals to develop cirrhosis in spite of intense fatty infiltration on a choline-deficient diet remains an anomaly (Buckley and Hartroft, 1955). Other workers have paid more attention to the presence of 'Mallory's hyaline' (Mallory, 1911). Edmondson, Peters, Reynolds, and Kuzma (1963) have drawn attention to the sclerosing hyaline necrosis which they noted to be more intense in the centrilobular zones of the livers of chronic alcoholics with acute liver disease. They considered that the acute lesion, if severe enough and repeated frequently enough, could result in portal cirrhosis. Similarly, Thaler (1962) considered that alcoholic cirrhosis was the result of repeated necrosis, in spite of the striking accumulation of fat in acute cases. Shorter and Baggenstoss (1959), in studying the histogenesis of cirrhosis in chronic alcoholism, were very impressed with the presence of alcoholic hyaline degeneration and necrosis, and found no real evidence that fatty cysts were important. Inflammatory reaction was marked around areas of hyaline degeneration but was absent around fatty cysts. They suggested that the failure of the liver to regenerate normally might be due to damage to the reticulin framework. 'Acute alcoholic hepatitis' is one of the terms given to an acute illness associated with excessive alcohol intake (Phillips and Davidson, 1954; Beckett, Livingstone, and Hill, 1961). The fully developed condition carries a poor prognosis, but the clinical picture is variable, some cases resembling extra-hepatic biliary obstruction (Phillips and Davidson, 1957) while in others the illness may occur

without jaundice (Beckett, Livingstone, and Hill, 1962). Phillips and Davidson (1954) stressed the importance of Mallory's alcoholic hyaline with accompanying necrosis and cellular infiltration in the histological picture, whereas Beckett, Livingstone, and Hill (1961) were more impressed with fatty change proceeding to patchy necrosis with acute inflammatory reaction. The part played by acute alcoholic hepatitis in the development of cirrhosis is very difficult to determine, as remarkable recovery may occur following extensive liver damage in the patient who abstains from alcohol and takes an adequate diet (Davidson and MacDonald, 1962).

Until recently the majority of authors distinguished only between portal and post-necrotic cirrhosis (Mallory, 1911; Karsner, 1943; Ratnoff and Patek, 1955). The classification of Gall (1960a) is essentially similar to the one used here, although the terminology is somewhat different. Gall's post-hepatitic group corresponds to the coarsely nodular cirrhosis of this series, although no such aetiology is implicated in the histories of most of these patients. Coarsely nodular cirrhosis occurs most often in reformed alcoholics and a comparison can be made with the changes in liver morphology following the giving of choline to rats previously fed a choline-deficient diet (Ohta, Zaki, and Hoffbauer, 1963). Presumably most of these patients had finely nodular cirrhosis at the time they curtailed their heavy drinking and larger nodules developed subsequently.

Post-necrotic cirrhosis is less common than other varieties in alcoholics, but its occurrence is well documented (Baggenstoss and Stauffer, 1952; Ratnoff and Patek, 1955). Popper *et al.* (1960) and Rubin, Krus, and Popper (1962) have re-examined the problem recently. In the first report they studied 308 cases. Their criteria for post-necrotic cirrhosis were similar to those of the present series, although more emphasis was placed on cellular changes. They found that 85 out of 187 alcoholics (45%) had post-necrotic features, although none had gross deformity of the liver. When the individual features were considered it was found that fatty metamorphosis and hyaline degeneration were much less common in the alcoholic post-necrotic cases than in the portal cases. Most difficulty was encountered when the question of collapse was considered. Collapse was most frequent in cases of frank post-necrotic cirrhosis. In 59 of the 85 cases, all three tabulated features of post-necrotic cirrhosis (large nodules, wide bands, with collapse cellular proliferation) were present, an incidence of 31.5% in the series. The suggestion was made that prolongation of the lives of some cirrhotics might be responsible for some of the cases of post-necrotic cirrhosis. The similar ages of survival of the three groups make it

unlikely that post-necrotic cirrhosis arises from either of the other types of cirrhosis. Miyai and Ruebner (1963) also found this explanation unsatisfactory in their study in which the ages of the patients with portal and post-necrotic cirrhosis were comparable. In their second paper (Rubin *et al.*, 1962) they attempted to determine the pathogenesis of post-necrotic cirrhosis in alcoholics. They concluded that post-necrotic cirrhosis could develop from portal cirrhosis as a result of continuing necrosis. Another suggestion has been to invoke other factors in the form of toxins or infection as a cause of post-necrotic cirrhosis in the alcoholic. In particular, anicteric hepatitis has been cited as a precursor. Klatzkin (1958) has provided the clearest evidence of the transition from anicteric hepatitis to post-necrotic cirrhosis, but his cases, like some other examples of post-necrotic cirrhosis following presumed viral hepatitis, were cases in which there was a continuing illness apparently beginning as typical viral hepatitis and ending as post-necrotic cirrhosis. The real problem is whether previous viral hepatitis, either anicteric or overt, can result, years later, in post-necrotic cirrhosis. Howard and Watson (1947) demonstrated an increased incidence of previous jaundice in patients with cirrhosis but Zieve, Hill, Nesbitt, and Zieve (1953) failed to find an 'increased incidence of residuals' in patients who had had viral hepatitis when compared with two groups, one who had been in an area where the disease had been epidemic without developing jaundice, and one which had not been in an epidemic area. An investigation into the same problem by Kunkel and Labby (1950) also failed to show a significant incidence of cirrhosis after viral hepatitis. Neefe, Norris, Reinhold, Mitchell, and Howell (1954) made a very interesting contribution in studying a group of patients whose donor blood had resulted in serum hepatitis. They found abnormal liver function tests and/or established liver damage in the patients, some of whom were alcoholic. This raised the question whether chronic or recurrent viraemia could contribute to alcoholic cirrhosis. MacDonald and Mallory (1958) found an apparently increased incidence of post-necrotic cirrhosis in patients who had had a course of arsenic, bismuth, or mercury injections as treatment for venereal disease. They suggested the possibility of anicteric serum hepatitis to explain the development of post-necrotic cirrhosis in their cases. Thirty-five per cent of their 221 cases were chronic users of alcohol, and some of these had features of alcoholic nutritional cirrhosis. No excess incidence of hepatoma was seen in either alcoholics or non-alcoholics. Baggenstoss and Stauffer (1952) compared two groups of patients with cirrhosis, one with a history of alcoholism and the other with a

history suggestive of viral hepatitis. The majority of the alcoholics had finely nodular cirrhosis, although out of 43, four had features of post-necrotic cirrhosis. There is no doubt that post-necrotic cirrhosis can occur without previous overt viral hepatitis and the part played by anicteric hepatitis in these circumstances is not known. In this series there are 18 cases of post-necrotic cirrhosis and only one gave a history suggestive of previous viral hepatitis.

In this series the most important factor in determining the presence of hepatoma in a case of cirrhosis associated with alcoholism was increasing age. Presumably, increased survival was related to more prolonged disease and this also correlated with the increased incidence of hepatoma in patients who gave up drinking some time before death. Alternatively, continued heavy drinking and poor nutrition may have an inhibitory effect on the development of hepatoma; subsequently, when liver disease is established and with the substitution of a nutritious diet and a reduced alcohol intake, circumstances may be more favourable for the development of hepatoma, either spontaneously or in response to carcinogens. Primary hepatic tumours have been noted in experimental animals maintained on diets deficient in choline (Copeland and Salmon, 1946; Salmon and Copeland, 1954) and various food factors, notably riboflavine, lessen the incidence of hepatic tumours in animals given carcinogens (Kensler, Sagiura, Young, Halter, and Rhoads, 1941).

In man it has been noted that hepatoma is common in populations and areas where nutrition is poor. Berman (1935) drew attention to the frequency of hepatoma in Bantus and later gathered the observations in many races in a classical monograph (Berman, 1951). Hepatoma is found to be common in China (Wu and Kang, 1930; Chung and Ch'en, 1957), Japan (Ishibashi and Takatsu, 1915), Java (Bonne, 1935), India (Rogers, 1925), the Philippines (Smith, 1926), and in Thailand (Viranuvatti and Satapanakul, 1958) in the races native to these countries. This is in marked contrast to the low incidence of hepatoma in the white races of the western hemisphere, whether they live at home or in an area where hepatoma is common among the natives (Strachan, 1934; Higginson, 1963). The incidence appears to be higher in the oriental and negro races in North America than in the white population but less high than in the same ethnic groups in their native countries (Berman, 1951). Berman drew attention to the variations in incidence in the Bantus in different parts of Africa found by himself and other workers (Prates, 1940). Such variations within the same ethnic groups suggest the likelihood that environmental factors, apart from

malnutrition, are operative in the aetiology of hepatoma (Higginson, 1963).

An increase in the incidence of hepatoma in recent years in the United States has been suggested (MacDonald, 1957; Greene and Schiff, 1961; Wells and Lundberg, 1963; Miyai and Ruebner, 1963; Patton and Horn, 1964) and this has been related to a similar increased incidence of healed acute yellow atrophy. Gall (1960b), Sagebiel, McFarland, and Taft (1963), and Patton and Horn (1964) observed a higher incidence of hepatoma in post-necrotic and post-hepatic cirrhosis than in nutritional cirrhosis, a point confirmed in the present series as far as the coarsely nodular group is concerned. Kay (1964) found only two cases of previous hepatitis on reviewing the records of 96 patients with hepatoma. Walshe and Wolff (1952) reported two patients with hepatomas occurring in post-necrotic cirrhosis seven years after attacks of serum hepatitis associated with nearsphenamine administration. Wells and Lundberg (1963) reported a high proportion of post-necrotic cases in their series of hepatoma, and questioned the possibility of anti-luetic therapy as an important factor. Hepatomas have been related to previous viral hepatitis (Steiner, 1960b; Sherlock, 1963; Miyai and Ruebner, 1963). Of four cases of previous viral hepatitis in the present series, one had a hepatoma.

SUMMARY

Eighty-four cases of cirrhosis in alcoholics coming to necropsy at the London Hospital between 1914 and 1963 have been studied. Finely nodular cirrhosis was the commonest single morphological type, but half the cases had either coarsely nodular or post-necrotic cirrhosis. Patients who continued drinking to death were more likely to have finely nodular cirrhosis and those who gave up drinking some time before death were more likely to have coarsely nodular cirrhosis. Post-necrotic cirrhosis appeared not to be influenced by this factor. Hepatoma was common, occurring in 25 of the 84 cases (30%). Its occurrence was most closely correlated with increased age and, as in most reported series, was commoner in men. There was a high incidence of hepatoma in patients who gave up drinking some time before death and correspondingly coarsely nodular cirrhosis was the variety with the highest proportion of cases with hepatoma. There were 18 cases of post-necrotic cirrhosis, only one of which gave a history of viral hepatitis. Only three patients with post-necrotic cirrhosis had hepatomas (17.6%), the lowest incidence in the three morphological varieties.

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